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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,052	07/14/2003	Yasumichi Hitoshi	7946-79800-01	7655
74839	7590	02/06/2008		
Klarquist Sparkman, LLP 121 SW Salmon St Floor 16 Portland, OR 97204			EXAMINER HALVORSON, MARK	
			ART UNIT	PAPER NUMBER
			1642	
			MAIL DATE	DELIVERY MODE
			02/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/620,052	HITOSHI ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 20 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 16-22 is/are pending in the application.
- 4a) Of the above claim(s) 3-6, 17 and 19-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 7, 16 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1-7 and 16-22 are pending.

Claim 3-6, 17 and 19-22 have been withdrawn.

Claims 1, 2, 7, 16 and 18 are under currently under examination.

The Final Rejection of 10 May 2006 is hereby withdrawn. Prosecution on the merits of this application is reopened on claims 1, 2, 7, 16 and 18 considered unpatentable for the reasons indicated below:

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 7, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington et al (cited previously) in view of Wang et al (US Patent No: 6,531,479 issued March 11, 2003, filing date March 29, 2001).

The claims are drawn to a method for identifying a compound that modulates cell cycle arrest, the method comprising contacting a cell comprising a target compound consisting of a flap structure specific endonuclease 1 (FEN1) and determining the chemical or phenotypic effect of the compound upon the cell, wherein the cell is an A549 cell, thereby identifying a compound that modulates cell cycle arrest wherein modulation is activation of cancer cell cycle arrest, wherein the polypeptide is recombinant, wherein the polypeptide is encoded by a nucleic acid comprising SEQ ID NO:13, wherein the compound is a small organic molecule.

Harrington et al disclose a method for identifying modulating agents of the FEN-1 peptide of SEQ ID NO:14 (see Sequence Search) which reduce the cell's capacity to repair DNA damage or inhibit endogenously naturally-occurring FEN1 (column 39 lines 25-28). These modulating agent are candidate neoplastic agents which can be tested further for antineoplastic activity. Harrington et al further disclose that the present invention may be used to design drugs that inhibit the binding of FEN1 to DNA flaps or nicks and to catalyze nuclease activity on the flap strand (column 42 lines 58-61). The nucleic acid of SEQ ID NO:13 encodes the peptide of SEQ ID NO:14.

In addition Harrington et al teach a recombinant FIN1 polypeptide used in a yeast two hybrid system to detect compounds that bind to FIN1 to identify candidate FEN-1 modulatory agents. (column 36 line 62 to column 39 line 24). Enzymatic activity is used to detect binding of a compound to FIN1 (Id).

Harrington et al does not teach an A549 cell.

Wang et al disclose that A549 cells and Hela cell can be used to measure the ability of compounds to inhibit the cell cycle (column 20, lines 2-8).

One of ordinary skill in the art would have motivated to substitute Wang et al's A549 cell for Harrington's Hela cell because Wang et al disclose that A549 cells and Hela cell can be used interchangeable to measure the ability of compounds to inhibit the cell cycle (column 20, lines 2-8). It would have been prima facie obvious to substitute Harrington's Hela cell with Wang et al's A549 cell to measure the effect of compounds on the inhibition of the cell cycle.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington et al in view of Wang, and further in view of Shibata et al (cited previously).

Claim 2 is drawn to method for identifying a compound that modulates cell cycle arrest, the method comprising contacting a cell comprising a target compound consisting of a flap structure specific endonuclease 1 (FEN1) and determining the chemical or phenotypic effect of the compound upon the cell, thereby identifying a compound that modulates cell cycle arrest, wherein the cell cycle effect of the compound is compared to the effect of the compound on a cell comprising a dominant negative mutant FEN1 polypeptide.

Wang et al and Harrington et al has been described supra.

Wang et al and Harrington et al does not specifically teach dominant negative mutant FEN1 polypeptides.

Shibata et al teach that expression of dominant negative FEN1 mutants results in the alteration of cell cycle checkpoint protein levels.

One of ordinary skill in the art would have been motivated to apply Shibata et al's negative FEN1 mutant proteins to Wang et al and Harrington et al's method for identifying a compound that modulates cell cycle arrest because Harrington et al describes FEN-1 mutants wherein the native protein has at least one amino acid deleted or replaced by another amino acid and the mutants exhibiting altered biological activity (column 32, lines 5-9).

It would have been prima facie obvious to one skilled in the art to have combined Shibata et al's negative FEN1 mutant proteins with Wang et al and Harrington et al's method for identifying a compound that modulates cell cycle arrest to determine the effect of the compound upon FEN1 dependent cell proliferation.

### ***Summary***

Claims 1, 2, 7, 16 and 18 stand rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at (571) 272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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